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None

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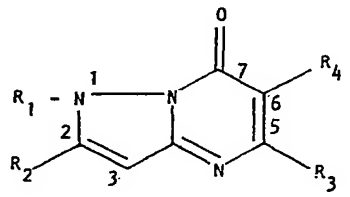
C2C

(54) 1H, 7H-pyrazolo1, 5-a pyrimidine-7-one derivatives and process for their preparation

(57) 1H, 7H-Pyrazolo[1,5-a]pyrimidine-7-one derivatives of formula (I)



(I)

wherein

R_1 is:

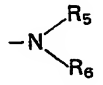
a) C_1-C_6 alkyl or benzyl;

b) pyridyl, unsubstituted or substituted by C_1-C_6 alkyl;

c) phenyl, unsubstituted or substituted by one or more substituents chosen from halogen, trihalo-methyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, formyloxy, C_2-C_6 alkanoyloxy, nitro, amino, formylamino and C_2-C_6 alkanoylamino;

R_2 is a) pyridyl; or b) phenyl, unsubstituted or substituted by one or more substituents chosen from halogen, trihalomethyl, nitro, C_1-C_6 alkoxy and C_1-C_6 alkyl;

R_3 is hydrogen or C_1-C_6 alkyl, unsubstituted or substituted by one or more substituents chosen from halogen, hydroxy, C_1-C_6 alkoxy, formyloxy, C_2-C_6 alkanoyloxy and the



group, wherein each of R_5 and R_6 is independently hydrogen, C_1-C_6 alkyl, phenyl or benzyl, or R_5 and R_6, taken together with the nitrogen atom to which they are linked, form a heterocyclic ring chosen from N-imidazolyl, hexahydro-N-azepinyl, N-pyrrolidinyl, N-piperazinyl, piperidino, thiomorpholino and morpholino, each of the heterocyclic rings being unsubstituted or substituted by C_1-C_6 alkyl;

R_4 is hydrogen, halogen, C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, C_3-C_4 alkenoyloxy, formyloxy or C_2-C_6 alkanoyloxy; and the pharmaceutically acceptable salts thereof; are *central nervous system depressants.*

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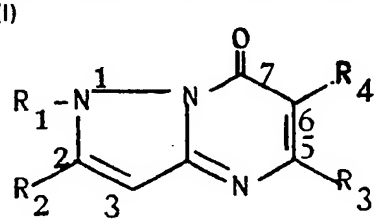
SPECIFICATION

1H,7H-Pyrazolo[1,5-a]pyrimidine-7-one derivatives and process for their preparation

The present invention relates to new 1H,7H-pyrazolo[1,5-a]pyrimidine-7-one derivatives, to a process for their preparation and to pharmaceutical compositions containing them. The invention provides compounds having the following general formula (I)



(I)

wherein

R_1 is:

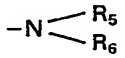
a) C_1-C_6 alkyl or benzyl;

b) pyridyl, unsubstituted or substituted by C_1-C_6 alkyl;

c) phenyl, unsubstituted or substituted by one or more substituents chosen from halogen, trihalo-methyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, formyloxy, C_2-C_6 alkanoyloxy, nitro, amino, formylamino and C_2-C_6 alkanoylamino;

R_2 is a) pyridyl; or b) phenyl, unsubstituted or substituted by one or more substituents chosen from halogen, trihalomethyl, nitro, C_1-C_6 alkoxy and C_1-C_6 alkyl;

R_3 is hydrogen or C_1-C_6 alkyl, unsubstituted or substituted by one or more substituents chosen from halogen, hydroxy, C_1-C_6 alkoxy, formyloxy, C_2-C_6 alkanoyloxy and the



group, wherein each of R_5 and R_6 is independently hydrogen, C_1-C_6 alkyl, phenyl or benzyl, or R_5 and R_6, taken together with the nitrogen atom to which they are linked, form a heterocyclic ring chosen from N-imidazolyl, hexahydro-N-azepinyl, N-pyrrolidinyl, N-piperazinyl, piperidino, thiomorpholino and morpholino, each of the heterocyclic rings being unsubstituted or substituted by C_1-C_6 alkyl;

R_4 is hydrogen, halogen, C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, C_3-C_4 alkenoyloxy, formyloxy or C_2-C_6 alkanoyloxy;

and the pharmaceutically acceptable salts thereof.

The present invention includes also the metabolites and the metabolic precursor of the compounds of formula (I) and all the possible isomers of the compounds of formula (I), e.g. optical isomers, and the mixtures thereof.

The alkyl, alkoxy, alkanoyloxy and alkanoylamino groups may be branched or straight chain groups.

A halogen atom is, for example, chlorine, bromine or fluorine, preferably it is chlorine or fluorine.

A trihalomethyl group is preferably a trifluoromethyl groups.

A C_2-C_6 alkanoyloxy group is, for example, acetoxy, propionyloxy, butyryloxy or valeryloxy, preferably it is acetoxy.

A C_1-C_6 alkyl group is preferably a C_1-C_4 alkyl group, in particular, methyl, ethyl, propyl or tert.butyl.

A C_1-C_6 alkoxy group is preferably C_1-C_4 alkoxy, in particular, methoxy, ethoxy, propoxy or butoxy.

A C_2-C_6 alkanoylamino group is, for example, acetylamino, propionylamino, butyrylamino or valerylamino; preferably it is acetylamino.

When R_1 and/or R_2 is phenyl, substituted as defined above, or R_3 is C_1-C_6 alkyl, substituted as defined above, they are preferably substituted by one, two or three substituents.

When R_1 is a C_1-C_6 alkyl group, it is, for example, methyl, ethyl, propyl, isopropyl, butyl, isobutyl or tert-butyl, preferably it is methyl, ethyl, propyl or tert-butyl.

When R_1 is a pyridyl group substituted by a C_1-C_6 alkyl group, the alkyl group may be, for example, methyl, ethyl or propyl, preferably it is methyl.

When R_1 and/or R_2 is a phenyl ring substituted as defined above, it is more preferably substituted by one or two substituents chosen from halogen, nitro, trifluoromethyl, C_1-C_4 alkyl and C_1-C_4 alkoxy.

When R_3 and/or R_4 is an unsubstituted C_1-C_6 alkyl group, it is, for example, methyl, ethyl, propyl, isopropyl or butyl, preferably it is methyl, ethyl, propyl or isopropyl.

When R_3 is a C_1-C_6 alkyl group substituted by one or more halogen atoms, it is preferably a C_1-C_3 alkyl group substituted by one to three chlorine or fluorine atoms.

When R_3 is a C_1-C_6 alkyl group substituted by one or more C_1-C_6 alkoxy groups, it is preferably a C_1-C_3 alkyl group substituted by one to three C_1-C_2 alkoxy group.

When R_4 is a halogen atom it is, e.g., chlorine, bromine or fluorine, preferably it is chlorine or bromine.

When R_4 is a C_1-C_6 alkoxy group, it is, for example, methoxy, ethoxy, propoxy, isopropoxy or butoxy, preferably it is methoxy, ethoxy or propoxy.

When one or both of R_5 and R_6, being the same or different, is a C_1-C_6 alkyl group, it is for example methyl, ethyl, propyl, isopropyl or butyl; preferably it is methyl, ethyl, propyl or isopropyl.

When R_5 and R_6, taken together with the nitrogen atom to which they are linked, form a heterocyclic ring as defined above and said ring is substituted by C_1-C_6 alkyl,

the alkyl group is preferably C_1-C_4 alkyl, in particular methyl or ethyl.

Preferred compounds of the invention are those of formula (I) wherein

R_1 is:

a') C_1-C_4 alkyl or benzyl;

b') pyridyl, unsubstituted or substituted by one or two substituents chosen from halogen, trifluoromethyl, C_1-C_4 alkyl, C_1-C_4 alkoxy, nitro, amino, formylamino and C_2-C_6 alkanoylamino;

R_2 is phenyl, unsubstituted or substituted by one or two substituents chosen from chlorine, fluorine, trifluoromethyl, nitro, C_1-C_4 alkyl and C_1-C_4 alkoxy;

R_3 is hydrogen or C_1-C_4 alkyl, unsubstituted or substituted by one to three substituents chosen from chlorine, fluorine, hydroxy, C_1-C_4 alkoxy, formyloxy, C_2-C_6 alkanoyloxy and the

$$-N\begin{matrix}R_5\\R_6\end{matrix}$$

group wherein each of R_5 and R_6 is independently hydrogen, C_1-C_4 alkyl or phenyl, or R_5 and R_6 taken together with the nitrogen atom to which they are linked, form a heterocyclic ring chosen from N-imidazolyl, hexahydro-N-azepinyl, N-pyrrolidinyl, N-piperazinyl, piperidino, thiomorpholino and morpholino, each of the heterocyclic rings being unsubstituted or substituted by C_1-C_3 alkyl;

R_4 is hydrogen, halogen, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, C_3-C_4 alkenyloxy or C_2-C_6 alkanoyloxy; and the pharmaceutically acceptable salts thereof.

More preferred compounds of the invention are those of formula (I) wherein

R_1 is:

a") C_1-C_4 alkyl, benzyl or pyridyl;

b") phenyl, unsubstituted or substituted by one or two substituents chosen from chlorine, fluorine, trifluoromethyl, methyl, C_1-C_2 alkoxy, nitro, amino, formylamino and C_2-C_4 alkanoylamino;

R_2 is phenyl, unsubstituted or substituted by one or two substituents chosen from halogen, trifluoromethyl, nitro, C_1-C_4 alkyl and C_1-C_4 alkoxy;

R_3 is hydrogen or C_1-C_4 alkyl, unsubstituted or substituted by one to three substituents chosen from halogen, hydroxy, C_1-C_2 alkoy, formyloxy, C_2-C_4 alkanoyloxy and the

$$-N\begin{matrix}R_5\\R_6\end{matrix}$$

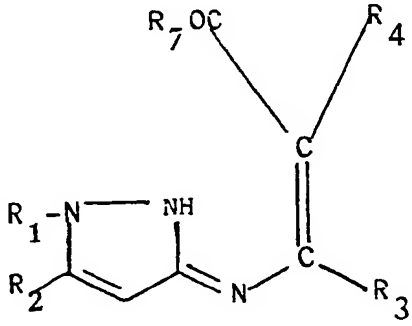
group, wherein each of R_5 and R_6 is independently hydrogen or C_1-C_4 alkyl, or R_5 and R_6, taken together with nitrogen atom to which they are linked, form a heterocyclic ring chosen from unsubstituted N-imidazolyl, unsubstituted hexahydro-N-azepinyl, unsubstituted N-pyrrolidinyl, N-piperazinyl unsubstituted or substituted by C_1-C_3 alkyl, piperidino and morpholino, each being unsubstituted or substituted by methyl and unsubstituted thiomorpholino; R_4 is hydrogen, halogen, C_1-C_4 alkyl, hydroxy, C_1-C_3 alkoxy, allyloxy or C_2-C_4 alkanoyloxy; and the pharmaceutically acceptable salts thereof.

Examples of pharmaceutically acceptable salts are the salts with inorganic acids, e.g. nitric, hydrochloric, hydrobromic and sulphuric acids and the salts with organic acid, e.g. citric, tartaric, maleic, malic, fumaric, methanesulphonic and ethanesulphonic acids.

Examples of particularly preferred compounds of the invention are:
1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-1-(4-methyl-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-1-(4-nitro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-fluoro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(3-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-benzyl-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-tert.butyl-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,5-dimethyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(2-pyridyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(3-pyridyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-bis-(3-chloro-phenyl)-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-2-(4-methoxy-phenyl)-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5,6-dimethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-6-methoxy-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-6-ethoxy-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-(N,N-diethylamino-methyl)-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-(pyrrolidin-1-yl-methyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-(imidazol-1-yl-methyl)-1H,7H-pyrazolo1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-methoxymethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
and the pharmaceutically acceptable salts thereof.

The compounds of the invention can be prepared by a process comprising:

a) cyclization of a compound of formula (II)

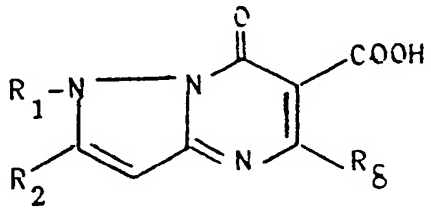


(II)

wherein

R_1, R_2, R_3 and R_4 are as defined above and R_7 is a nucleophile group which is capable of being cleaved from the carbon atom to which it is attached during the cyclisation of the compound of formula (II), or a salt thereof;

b) decarboxylation of a compound of formula (III)

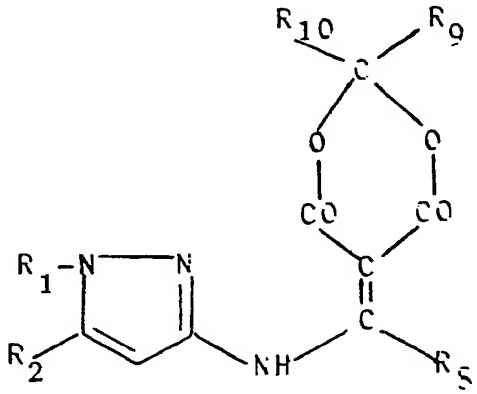


(III)

wherein

R_1 and R_2 are as defined above and R_8 is hydrogen or unsubstituted C_1-C_6 alkyl, so obtaining compounds of formula (I) wherein R_3 is hydrogen or unsubstituted C_1-C_6 alkyl and $_4$ is hydrogen, or

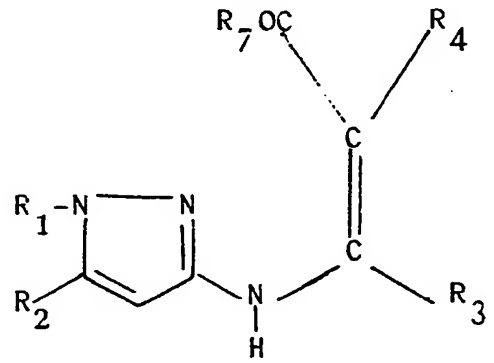
c) thermal cyclisation of a compound of formula (IV)



(IV)

wherein R_1, R_2 and R_8 are as defined above and each of R_9 and R_{10} is independently C_1-C_6 alkyl, so obtaining compounds of formula (I) wherein R_3 is hydrogen or unsubstituted C_1-C_6 alkyl and R_4 is hydrogen, and if desired, converting a compound of formula (I) into another compound of formula (I) and/or, if desired, converting a compound of formula (I) into a pharmaceutically acceptable salt thereof and/or, if desired, obtaining a free compound of formula (I) from a salt thereof and/or, if desired, separating a mixture of isomers into the single isomers. When R_7 is a nucleophile group as defined above, it is, for example, hydroxy, tri-(C_1-C_6)alkyl-silyloxy, or C_1-C_6 alkoxy.

The compounds of formula (II) may also be represented by the tautomeric formula (IIa)



(IIa)

wherein

R_1, R_2, R_3, R_4 and R_7 are as defined above.

Preferred salts of the compounds of formula (II) are, for example, those with inorganic acids such as hydrochloric, hydrobromic, hydroiodic, phosphoric and sulphuric acid.

The cyclization of a compound of formula (II) may be, for example, carried out by treatment with an acid condensing agent such as polyphosphoric acid (alone or in the presence of phorphorus oxychloride), sulphuric acid, hydrochloric acid, methanesulphonic acid or p-toluenesulphonic acid, at a temperature ranging preferably between about 50°C and about 150°C; the reaction may be carried out in an organic solvent such as dimethylformamide, dimethylacetamide, dimethylsulphoxide, benzene, toluene, xylene, ethylene glycol monomethylether or dichloroethane, but it is preferably carried out in the absence of a solvent.

Alternatively, the cyclization of a compound of formula (II) may be carried out by heating the compound at a temperature ranging between about 150°C and about 350°C, preferably between 200°C and 300°C, in an inert high boiling organic solvent such as diphenyl ether, or in the absence of a solvent.

The decarboxylation of a compound of formula (III) may be, for example, carried out by heating in a solvent such as quinoline in the presence of copper powder at a temperature varying between 150°C and 200°C, or alternatively by melting in the presence of CuO at a temperature varying between 200°C and 300°C.

The termal cyclization of a compound of formula (IV) may be, for example, carried out by melting or alternatively by heating in an inert solvent such as nitrobenzene, diethylphthalate mineral oil, diphenyl ether or Dowtherm A (eutectic mixture of diphenyl and diphenyl ether), at a temperature varying between 200°C and 300°C, preferably varying between 230°C and 270°C.

A compound of formula (I) may be converted, as stated above, into another compound of formula (I) by known methods: for example, free hydroxy groups may be etherified by reacting with a suitable alkyl halide in the presence of a base such as NaOH, KOH, Na_2CO_3, NaH, $NaNH_2$, sodium methoxide, K_2CO_3 or sodium ethoxide, in a solvent selected from the group consisting, for example, of methanol, ethanol, dioxane, acetone, dimethylformamide, hexamethylphosphorotriamide, tetrahydrofuran, water and their mixtures at a temperature ranging preferably between about 0°C and about 150°C.

Furthermore the etherified hydroxy groups may be converted into free hydroxy groups, for example, by treatment with pyridine hydrochloride or with a strong acid such as HCl, HBr, or HI, or with a Lewis acid such as $AlCl_3$ or BBr_3. Furthermore, for example, a nitro group may be converted into an amino group by treatment, for example, with stanous chloride in concentrated hydrochloric acid, using, if necessary, an organic cosolvent such as acetic acid, dioxane, tetrahydrofuran at a temperature varying between room temperature and about 100°C.

Furthermore, for example, an amino or hydroxy group may be converted respectively into a formylamino, C_2-C_6 alkanoylamino or C_2-C_6 alkanoyloxy group, for example by reaction with formic acid or with the corresponding alkanoyl anhydride without any solvent or in an organic solvent such as dioxane, dimethylformamide, tetrahydrofuran, usually in the presence of a base such as pyridine or triethylamine at a temperature varying between 0°C and about 100°C.

Furthermore, for example, a compound of formula (I) wherein R_4 is hydrogen may be converted into a compound of formula (I) wherein R_4 is chlorine or bromine by reaction with a suitable halogenating agent such as chlorosuccinimide or bromosuccinimide, SO_2Cl_2 or pyridinium bromide perbromide, operating at a temperature ranging from 0°C to 100°C and using, for example, as solvent CCl_4 or dichloroethane in the reaction with SO_2Cl_2, pyridine in the reaction with pyridinium bromide perbromide and benzene in the reaction with a halosuccinimide.

Furthermore, for example, a compound of formula (I) wherein R_3 is a C_1-C_6 alkyl group substituted by a halogen atom may be converted into a compound of formula (I) wherein R_3 is a C_1-C_6 alkyl group substituted by a group

$$-N\begin{matrix}R_5\\R_6\end{matrix},$$

wherein R_5 and R_6 are as defined above, by reaction with a compound of formula

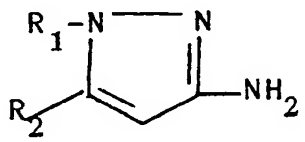
$$HN\begin{matrix}R_5\\R_6\end{matrix},$$

wherein R_5 and R_6 are as defined above, in an organic solvent such as methylethylketone, toluene, xylene, dimethylformamide, dimethylacetamide, at a temperature varying between 20°C and 150°C.

Also the optional salification of a compound of formula (I) as well as the conversion of a salt into a free compound and the separation of a mixture of isomers into the single isomers may be carried out by conventional methods.

For example, the separation of a mixture of optical isomers into the individual isomers may be carried out by salification with an optically active base or acid and subsequent fractional crystallization.

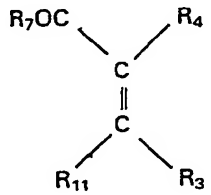
The compounds of formula (II) may be prepared, for example, by reacting a compound of formula (V)



(V)

wherein

R_1 and R_2 are as defined above, or a salt thereof, with a compound of formula (VI)



(VI)

wherein

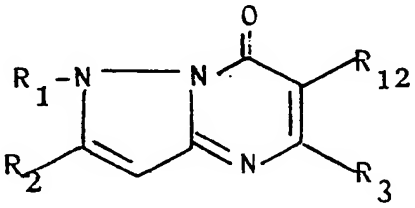
R_3, R_4 and R_7 are as defined above and R_{11} is a reactive group chosen, preferably, from hydroxy, amino, C_1-C_6 alkoxy, or tri-(C_1-C_6)alkyl-silyloxy.

Preferred salts of a compound of formula (V) are, for example, those with inorganic acids such as hydrochloric, hydrobromic, phosphoric and sulphuric acid.

The reaction between a compound of formula (V) and a compound of formula (VI) may be carried out, for example, by heating in solvents such as dioxane, toluene, xylene, acetonitrile, C_1-C_4 alkyl alcohols, acetic acid, dimethylformamide, dimethylacetamide, diphenylether or in the absence of a solvent, at a temperature varying from room temperature to about 200°C. Preferably, when R_{11} is hydroxy, the reaction between a compound of formula (V) and a compound of formula (VI) is carried out in the presence of an acid condensing agent such as polyphosphoric acid, methanesulphonic acid, p-toluenesulphonic acid or acetic acid using the same experimental conditions, as described above, for the cyclization of the compounds of formula (II).

Under these specific conditions the reaction of a compound of formula (V) with a compound of formula (VI) may be carried out till a compound of formula (I) is obtained without the need to isolate the intermediate product of formula (II) formed during the reaction.

The compounds of formula (III) may be prepared, for example, by hydrolyzing a compound of formula (VII)



(VII)

wherein

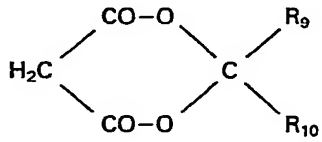
R_1, R_2 and R_3 are as defined above and R_{12} is cyano or an esterified carboxy group or a tri-(C_1-C_6)alkyl-silyloxy-carbonyl group, by treatment, for example, with a mineral acid such as HCl, HBr, HI in water or in acetic acid or dioxane or their mixtures at a temperature varying between room temperature and about 120°C.

The compounds of formula (IV) may be prepared, for example, by reacting a compound of formula (V) with the mixture of a compound of formula (VIII)

$$R_8-C(OR_{13})_3 \qquad \text{(VIII)}$$

wherein

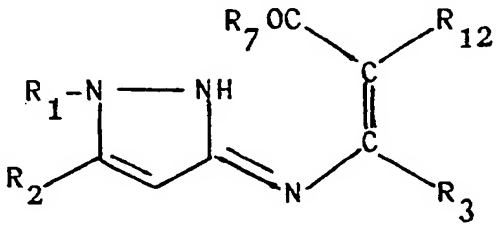
R_8 is as defined above and R_{13} is C_1-C_6 alkyl, and a compound of formula (IX)



(IX)

wherein

R_9 and R_{10} are as defined above. The reaction between a compound of formula (IV) and the mixture of a compound of formula (VIII) and a compound of formula (IX), may be carried out, for example, without a solvent or in the presence of an inert solvent such as benzene, ethanol, dioxane, tetrahydrofuran, acetonitrile, dimethylformamide, at a temperature varying between room temperature and about 150°C. The compound of formula (VIII) may be prepared by cyclizing a compound of formula (X)



(X)

wherein

R_1, R_2, R_3, R_7 and R_{12} are as defined above, using the same experimental conditions specified above for the cyclization of a compound of formula (II).

The compounds of formula (V), (VI), (VIII) and (IX) are known compounds or may be prepared by conventional methods: in some cases they are commercially available products. The compounds of the invention are active on the central nervous system (CNS), in particular as central nervous systems depressants, i.e. as sedative, anticonvulsive agents, minor tranquilizers, and as sleep-inducing agents. The activity on the CNS of the compounds of the invention was evaluated, for example, in the experimental framework of the behavioural assessment by the Irwin's technique [Irwin, S., Psychopharmacologia (Berl.), *13*, 222, 1968]. In this test, the compounds of the invention, proved to be active as CNS depressants, in particular as sedative agents and as minor tranquilizers, and in inducing hypnosis e.g. in mice and rats. The animals, treated with oral doses ranging from 5 to 100 mg/kg body weight, showed loss of righting reflex, without contemporary depression of muscle-tone, respiratory frequency, rectal temperature and of otherless indicative reflexes.

The toxicity of the compounds of the invention is negligible, therefore they can be safely used in therapy. Nine hours food deprived mice and rats were treated orally with single administration of increasing doses, then housed and normally fed. The orientative acute toxicity (LD_{50}) was assessed on the seventh day after the treatment and resulted, in general, higher than 600 mg/kg.

The compounds of the invention can be administered in a variety of dosage forms, e.g. orally, in the form of tablets, capsules, sugar or film coated tablets, liquid solutions or suspensions; rectally, in the form of suppositories; parenterally, e.g. intramuscularly, or by intravenous injection or infusion.

The dosage depends on the age, weight, conditions of the patient and administration route; for example the dosage adopted for oral administration to adult humans may range from about 10 to about 100 mg pro dose, from 1 to 5 times daily.

The invention includes pharmaceutical compositions comprising a compound of the invention in association with a pharmaceutically acceptable excipient (which can be a carrier or diluent).

The pharmaceutical compositions containing the compounds of the invention are usually prepared following conventional methods and are administered in a pharmaceutically suitable form.

For example, the solid oral forms may contain, together with the active compound, diluents, e.g., lactose, dextrose, saccharose, cellulose, corn starch or potato starch; lubricants, e.g. silica, talc, stearic acid, magneisum or calcium stearate, and/or polyethylene glycols; binding agents, e.g. starches, arabic gums, gelatin, methylcellulose, carboxymethyl cellulose or polyvinyl pyrrolidone; disaggregating agents, e.g. a starch, alginic acid, alginates or sodium starch glycolate; effervescing mixtures; dyestuffs; sweeteners; wetting agents, such as lecithin, polysorbates, laurylsulphates; and, in general, non-toxic and pharmacologically inactive substances used in pharmaceutical formulations. Said pharmaceutical preparations may be manufactured in known manner, for example, by means of mixing, granulating, tabletting, sugar-coating, or film-coating processes. The liquid dispersions for oral administration may be e.g. syrups, emulsions and suspensions.

The syrups may contain as carrier, for example, saccharose or saccharose with glycerine and/or mannitol and/or sorbitol; in particular a syrup to be administered to diabetic patients can contain as carriers only products not metabolizable to glucose, or metabolizable in very small amount to glucose, for example sorbitol.

The suspensions and the emulsions may contain as carrier, for example, a natural gum, agar, sodium alginate, pectin, methylcellulose, carboxymethylcellulose, or polyvinyl alcohol.

The suspensions or solutions for intramuscular injections may contain together with the active compound a pharmaceutically acceptable carrier, e.g. sterile water, olive oil, ethyl oleate, glycols, e.g. propylene glycol, and if desired, a suitable amount of lidocaine hydrochloride. The solutions for intavenous injections or infusions may contain as carrier, for example, sterile water or preferably they may be in the form of sterile, aqueous, isotonic saline solutions.

The suppositories may contain together with the active compound a pharmaceutically acceptable carrier, e.g. cocoa-butter, polyethylene glycol, a polyoxyethylene sorbitan fatty acid ester surfactant or lecithin.

The following examples illustrate but do not limit the invention.

Example 1

3-amino-1,5-diphenyl-pyrazole (5.2 g) was reacted with ethyl acetoacetate (4.4 g) in polyphosphoric acid (52 g: 28 g of H_3PO_4 and 24 g of P_2O_5) under stirring at 100°C for 1.5 hours. After cooling the reaction mixture was diluted with ice water and neutralized with 35% NaOH. The solution was extracted with ethyl acetate and then the organic phase was evaporated *in vacuo* to dryness. Crystallization from chloroform-isopropyl ether gave 2.5 g of 1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one, m.p. 147-148°C, NMR (CDC_3) δppm: 2.37(s) (3H, CH_3), 5.91 (bs) (1H, C-6 proton), 6.55 (s) (1H, C-3 proton), 7.40 (m) (10H, phenyl protons).

By proceeding analogously the following compounds were prepared:

5-methyl-1-(2-methylphenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-1-(2-nitro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(2-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(2,4-dichloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(2,5-dichloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(2-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-1-(3-methyl-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-1-(3-nitro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-methoxy-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(2,6-dichloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-fluoro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(3-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one, m.p. 149-150°C;
5-methyl-1-(4-methyl-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-1-(4-nitro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-fluoro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(4-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-benzyl-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-tert.butyl-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,5-dimethyl-2-phenyl-1H-7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(2-pyridyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(3-pyridyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
2-(4-chloro-phenyl)-1-phenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
2-(4-methoxy-phenyl)-1-phenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-1-phenyl-2-(3-pyridyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-bis-(3-chloro-phenyl)-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one; and
1-(3-chloro-phenyl)-2-(4-methoxy-phenyl)-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one.

Example 2

By proceeding according to Example 1, using suitable substituted acetoacetates, the following compounds were prepared:

1,2-diphenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one, m.p. 142-143°C;
1,2-diphenyl-6-ethyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-methyl-6-propyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-6-isopropyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5,6-dimethyl-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one, m.p. 208-210°C;
1,2-diphenyl-6-methoxy-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-6-ethoxy-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-6-hydroxy-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-acetoxy-1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-6-isopropoxy-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-methyl-6-propoxy-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-allyloxy-1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-ethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one,
1,2-diphenyl-5-propyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-isopropyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one-;
5-chloromethyl-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one, m.p. 138-140°C;
5-dichloromethyl-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-methoxymethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-ethoxymethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-diethoxymethyl-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-hydroxymethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-acetoxymethyl-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-methylphenyl)-2-phenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-nitro-phenyl)-2-phenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-chloro-phenyl)-2-phenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-2-phenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-fluoro-phenyl)-2-phenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
2-phenyl-5-trifluoromethyl-1-(3-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-bis-(3-chloro-phenyl)-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-2-(4-methoxy-phenyl)-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-5-methyl-1-(4-methyl-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-5-methyl-1-(4-nitro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-1-(4-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-1-(3-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-1-(4-fluoro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-5-methyl-2-phenyl-1-(3-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-1,2-bis-(3-chloro-phenyl)-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-1-(3-chloro-phenyl)-2-(4-methoxy-phenyl)-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5,6-dimethyl-1-(4-methyl-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5,6-dimethyl-1-(4-nitro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-chloro-phenyl)-5,6-dimethyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-5,6-dimethyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-fluoro-phenyl)-5,6-dimethyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5,6-dimethyl-2-phenyl-1-(3-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-bis-(3-chloro-phenyl)-5,6-dimethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-2-(4-methoxy-phenyl)-5,6-dimethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-methoxy-5-methyl-1-(4-methyl-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-methoxy-5-methyl-1-(4-nitro-phenyl)-2-phenyl-1H-7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-chloro-phenyl)-6-methoxy-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-6-methoxy-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-fluoro-phenyl)-6-methoxy-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-methoxy-5-methyl-2-phenyl-1-(3-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-bis-(3-chloro-phenyl)-6-methoxy-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one; and
1-(3-chloro-phenyl)-6-methoxy-2-(4-methoxy-phenyl)-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one.

Example 3

Isopropylidene-N-(1,2-diphenyl-pyrazol-3-yl)-amino-methylenemalonate, m.p. 235-237°C (3 g), dissolved in diphenylether (30 ml) was heated at the reflux temperature for 8 minutes. After cooling the solvent was distilled off *in vacuo* and the residue was purified over a flash column using ethyl acetate as eluent. The purified product was crystallized from CH_2Cl_2/isopropyl ether to give 0.9 g of 1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one, m.p. 146-148°C, NMR ($CDCl_3$) δ ppm: 5.91 (d) (1H, C-6 proton), 6.52 (s) (1H, C-3 proton), 7.22 (m) (10H, phenyl protons), 7.88 (d) (1H, C-5 proton).

By proceeding analogously the following compounds were prepared:
1-(4-methyl-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-nitro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-chloro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-fluoro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
2-phenyl-1-(3-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-benzyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-phenyl-2-(3-pyridyl)−1H,7H−pyrazolo[1,5-a]pyrimidine-7-one;
2-phenyl-1-(2-pyridyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-bis-(3-chloro-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one; and
1-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one.

Example 4

1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one (1.4 g) dissolved in benzene (50 ml) was reacted with N-bromo-succinimide (0.95 g) under stirring at room temperature for 2 hours. The precipitate was dissolved by adding chloroform and the solution was washed with water. Evaporation *in vacuo* to dryness and crystallization of the residue from chloroform/ispropy alcohol gave 1.6 g of 6-bromo-1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one.

By proceeding analogously the following compounds were prepared:
6-bromo-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-bromo-1,2-diphenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-bromo-5-methyl-1-(4-methyl-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-bromo-5-methyl-1-(4-nitro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-bromo-1-(4-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-bromo-1-(3-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-bromo-1-(4-fluoro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-bromo-5-methyl-2-phenyl-1-(3-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one; and
6-chloro-1,2-diphenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one.

Example 5

5-Methyl-1-(4-nitrophenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one (4 g) was reacted with $SnCl_2.2H_2O$ (25 g) in 37% HCl (15 ml) and acetic acid (45 ml) under stirring at 60°C for 2 hours. After cooling the precipitate was filtered and washed with water and then suspended under stirring in 2N NaOH: the product was filtered, washed with water until neutral and then crystallized from chloroform-ethanol to give 2.8 g of 1-(4-amino-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one.

By proceeding analogously the following compounds were prepared:
1-(4-amino-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-amino-phenyl)-2-phenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-amino-phenyl)-5,6-dimethyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-amino-phenyl)-6-chloro-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one; and
1-(4-amino-phenyl)-6-methoxy-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one.

Example 6

5-Chloromethyl-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one, m.p. 138-140°C, (2.2 g) was reacted with pyrrolidine (1 g) in 2-butanone (150 ml) at the reflux temperature for 16 hours. After cooling the solution was evaporated *in vacuo* to dryness and the residue was purified over a SiO_2 column using chloroform/methanol 97:3 as eluent. Crystallization of the recovered product from CH_2Cl_2-isopropyl ether gave 1.6 g of 1,2-diphenyl-5-(pyrrolidin-1-yl-methyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one.

By proceeding analogously the following compounds were prepared:
5-(N,N-diethylamino-methyl)-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-(morpholino-methyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-(N,N-dimethylamino-methyl)-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-(thiomorpholino-methyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-(N-isopropylamino-methyl)-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-(imidazol-1-yl-methyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-(N-tert.butylamino-methyl)-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-(piperidino-methyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-(hexahydro-1H-azepin-1-yl-methyl)-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one; and
1,2-diphenyl-5-[(4-methyl-piperazin-1-yl)-methyl]-1H,7H-pyrazol[1,5-a]pyrimidine-7-one.

Example 7

1-(4-Amino-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one (2g) was heated under stirring in acetic acid (30 ml) containing 37% HCl (5 ml) at 60°C for 1 hour. After cooling the precipitate was filtered and washed with acetic acid and then with water to give 1.9 g of 1-(4-amino-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one hydrochloride, m.p. > 350°C.

By proceeding analogously the following compounds were prepared:
1-(4-amino-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one hydrochloride; and
1-(4-amino-phenyl)-2-phenyl-5-trifluoromethyl-pyrazolo[1,5-a]pyrimidine-7-one hydrochloride.

Example 8

Tablets, each weighing 75 mg and containing 25 mg of the active substance are manufactured as following:

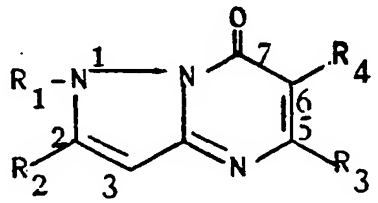
Compositions (for 10000 tablets)

1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one	250 g
Lactose	355 g
Corn starch	120 g
Talc powder	17.5 g
Magnesium stearate	7.5 g

1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one, lactose and a half of the corn starch are mixed; the mixture is then forced through a sieve of 0.5 mm openings. Corn starch (10 g) is suspended in warm water (100 ml). The resulting paste is used to granulate the powder. The granules are dried, comminuted on a sieve of sieve size 1.4 mm, then the remaining quantity of starch, talc and magnesium stearate is added, carefully mixed and processed into tablets using punches of 6 mm diameter.

CLAIMS

1. A compound of the following general formula (I)



(I)

wherein

R_1 is:

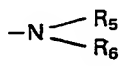
a) C_1-C_6 alkyl or benzyl;

b) pyridyl, unsubstituted or substituted by C_1-C_6 alkyl;

c) phenyl, unsubstituted or substituted by one or more substituents chosen from halogen, trihalo-methyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, formyloxy, C_2-C_6 alkanoyloxy, nitro, amino, formylamino and C_2-C_6 alkanoylamino;

R_2 is a) pyridyl; or b) phenyl, unsubstituted or substituted by one or more substituents chosen from halogen, trihalomethyl, nitro, C_1-C_6 alkoxy and C_1-C_6 alkyl;

R_3 is hydrogen or C_1-C_6 alkyl, unsubstituted or substituted by one or more substituents chosen from halogen, hydroxy, C_1-C_6 alkoxy, formyloxy, C_2-C_6 alkanoyloxy and the



group, wherein each of R_5 and R_6 is independently hydrogen, C_1-C_6 alkyl, phenyl or benzyl, or R_5 and R_6, taken together with the nitrogen atom to which they are linked, form a heterocyclic ring chosen from N-imidazolyl, hexahydro-N-azepinyl, N-pyrrolidinyl, N-piperazinyl, piperidino, thiomorpholino and morpholino, each of the heterocyclic rings being unsubstituted or substituted by C_1-C_6 alkyl;

R_4 is hydrogen, halogen, C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, C_3-C_4 alkenoyloxy, formyloxy or C_2-C_6 alkanoyloxy; and the pharmaceutically acceptable salts thereof.

2. A compound of formula (I), according to claim 1, wherein:

R_1 is:

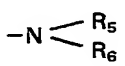
a') C_1-C_4 alkyl or benzyl;

b') pyridyl, unsubstituted or substituted by methyl;

c') phenyl, unsubstituted or substituted by one or two substituents chosen from halogen, trifluoromethyl, C_1-C_4 alkyl, C_1-C_4 alkoxy, nitro, amino, formylamino and C_2-C_6 alkanoylamino;

R_2 is phenyl, unsubstituted or substituted by one or two substituents chosen from chlorine, fluorine, trifluoromethyl, nitro, C_1-C_4 alkyl and C_1-C_4 alkoxy;

R_3 is hydrogen or C_1-C_4 alkyl, unsubstituted or substituted by one to three substituents chosen from chlorine, fluorine, hydroxy, C_1-C_4 alkoxy, formyloxy, C_2-C_6 alkanoyloxy and the



group wherein each of R_5 and R_6 is independently hydrogen, C_1-C_4 alkyl or phenyl, or R_5 and R_6 taken together with the nitrogen atom to which they are linked, form a heterocyclic ring chosen from N-imidazolyl, hexahydro-N-azepinyl, N-pyrrolidinyl, N-piperazinyl, piperidino, thiomorpholino and morpholino, each of the heterocyclic rings being unsubstituted or substituted by C_1-C_3 alkyl;

R_4 is hydrogen, halogen, C_1-C_4 alkyl, hydroxy,

C_1-C_4 alkoxy, C_3-C_4 alkenyloxy or C_2-C_6 alkanoyloxy; and the pharmaceutically acceptable salts thereof.

3. A compound of formula (I), according to claim 1, wherein:

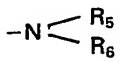
R_1 is:

a") C_1-C_4 alkyl, benzyl or pyridyl;

b") phenyl, unsubstituted or substituted by one or two substituents chosen from chlorine, fluorine, trifluoromethyl, methyl, C_1-C_2 alkoxy, nitro, amino, formylamino and C_2-C_4 alkanoylamino;

R_2 is phenyl, unsubstituted or substituted by one or two substituents chosen from halogen, trifluoromethyl, nitro, C_1-C_4 alkyl and C_1-C_4 alkoxy;

R_3 is hydrogen or C_1-C_4 alkyl, unsubstituted or substituted by one to three substituents chosen from halogen, hydroxy, C_1-C_2 alkoxy, formyloxy, C_2-C_4 alkanoyloxy and the



group, wherein each of R_5 and R_6 is independently hydrogen or C_1-C_4 alkyl, or R_5 and R_6, taken together with nitrogen atom to which they are linked, form a heterocyclic ring chosen from unsubstituted N-imidazolyl, unsubstituted hexahydro-N-azepinyl, unsubstituted N-pyrrolidinyl, N-piperazinyl unsubstituted or substituted by C_1-C_3 alkyl, piperidino and morpholino each being unsubstituted or substituted by methyl and unsubstituted thiomorpholino;

R_4 is hydrogen, halogen, C_1-C_4 alkyl, hydroxy, C_1-C_3 alkoxy, allyloxy or C_2-C_4 alkanoyloxy; and the pharmaceutically acceptable salts thereof.

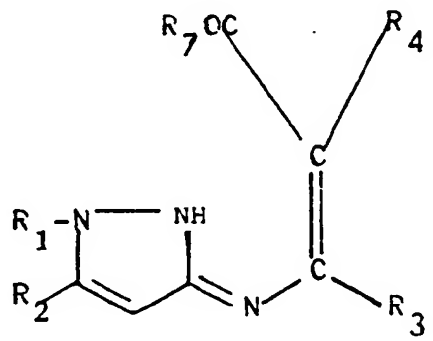
4. A compound selected from the group consisting of:

1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-trifluoromethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-1-(4-methyl-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-1-(4-nitro-phenyl)-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(4-fluoro-phenyl)-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(3-trifluoromethyl-phenyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-benzyl-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-tert.butyl-5-methyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,5-dimethyl-2-phenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(2-pyridyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-methyl-2-phenyl-1-(3-pyridyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-bis-(3-chloro-phenyl)-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1-(3-chloro-phenyl)-2-(4-methoxy-phenyl)-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5,6-dimethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
6-chloro-1,2-diphenyl-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidie-7-one;
1,2-diphenyl-6-methoxy-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-6-ethoxy-5-methyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
5-(N,N-diethylamino-methyl)-1,2-diphenyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-(pyrrolidin-1-yl-methyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-(imidazol-1-yl-methyl)-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;
1,2-diphenyl-5-methoxymethyl-1H,7H-pyrazolo[1,5-a]pyrimidine-7-one;

and the pharmaceutically acceptable salts thereof.

5. A process for the preparation of a compound of formula (I) and the pharmaceutically acceptable salts thereof, according to claim 1, the process comprising:

a) cyclization of a compound of formula (II)

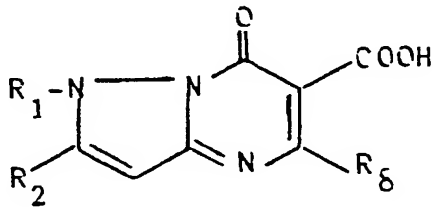


(II)

wherein

R_1, R_2, R_3 and R_4 are as defined in claim 1 and R_7 is a nucleophile group which is capable of being cleaved from the carbon atom to which it is attached during the cyclization of the compound of formula (II), or a salt thereof;

b) decarboxylation of a compound of formula (III)

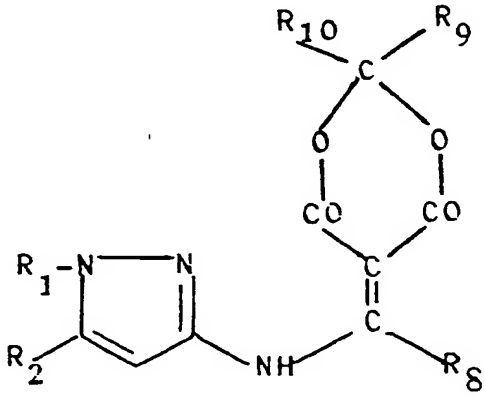


(III)

wherein

R_1 und R_2 are as defined in claim 1 and R_8 is hydrogen or unsubstituted C_1-C_6 alkyl, so obtaining compounds of formula (I) wherein R_3 is hydrogen or unsubstituted C_1-C_6 alkyl and R_4 is hydrogen, or

c) thermal cyclization of a compound of formula (IV)



(IV)

wherein

R_1 and R_2 are as defined in claim 1, R_8 is as defined above and each of R_9 and R_{10} is independently C_1-C_6 alkyl, so obtaining compounds of formula (I) wherein R_3 is hydrogen or unsubstituted C_1-C_6 alkyl and R_4 is hydrogen, and if desired, converting a compound of formula (I) into another compound of formula (I) and/or, if desired, converting a compound of formula (I) into a pharmaceutically acceptable salt thereof and/or, if desired, obtaining a free compound of formula (I) from a salt thereof and/or, if desired, separating a mixture of isomers into the single isomers.

6. A pharmaceutical composition containing a suitable carrier and/or diluent and, as an active principle, a compound of formula (I) according to claim 1, or a pharmaceutically acceptable salt thereof.

7. A compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt thereof, hereinbefore specified other than a compound or salt claimed in claim 4.

8. A compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt thereof, for use in a method of treatment of the human or animal body in therapy.

9. A compound of formula (I) or salt thereof according to claim 8 for use as a central nervous system depressant.

10. A process for the preparation of a compound of formula (I) as defined in claim 1, said process being substantially as hereinbefore described in any one of Examples 1 to 6.

11. A process for the preparation of a pharmaceutically acceptable salt of a compound of formula (I) as defined in claim 1, said process being substantially as hereinbefore described in Example 7.

12. A pharmaceutical composition substantially as hereinbefore described in Example 8.

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